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(FILE 'HOME' ENTERED AT 15:56:55 ON 23 NOV 2004)

FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 15:57:13 ON 23 NOV 2004

L1 28 S CONSTITUTIVELY AND ACTIVATED AND RECEPTOR AND TECHNOLOGY
L2 2 S L1 AND ORPHAN RECEPTOR

FILE 'STNGUIDE' ENTERED AT 15:59:23 ON 23 NOV 2004

L3 0 S ORPHAN RECEPTORS AND CART ASSAY

FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 16:02:46 ON 23 NOV 2004

L4 0 S ORPHAN RECEPTORS AND CART
L5 2134644 S RECEPTOR
L6 7893 S L5 AND ORPHAN
L7 3 S L6 AND CART

L7 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
 TI Filling the interstices: Ghrelin neurons plug several holes in regulation
 of energy balance.
 PY 2003
 SO Neuron, (February 20 2003) Vol. 37, No. 4, pp. 550-553. print.
 ISSN: 0896-6273 (ISSN print).

L7 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
 TI The **orphan** G-protein-coupled **receptor** ARE113 is a
 novel **receptor** target for obesity.
 PY 2000
 SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract
 No.-569.18. print.
 Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New
 Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
 ISSN: 0190-5295.

AB **Orphan** GPCRs are cloned proteins with characteristics common to
 the GPCR superfamily but no identified natural ligand(s) and consequently
 no identified function(s). Here we report that the **orphan** GPCR
 ARE113 may play a role in metabolism in rats. In situ hybridization
 analysis demonstrated that GPCR ARE113 is expressed in the arcuate and the
 ventromedial nuclei, two hypothalamic regions involved in metabolic
 regulation. Double labeling studies in the arcuate nucleus indicated that
 20% of GPCR ARE113 is co-localized with AGRP and NPY, two
receptors with orexigenic functions. Expression of GPCR ARE113
 was altered in food-deprived and genetically obese rats. Antisense
 oligonucleotides to GPCR ARE113 mRNA decreased body weight gain and
 feeding behavior in Sprague-Dawley rats. Using a ligand-independent assay
 (i.e. **CART**(R) technology), we have screened the ARE113
receptor against a small molecule chemical library and identified
 selective inverse agonists at GPCR ARE113. The lead in this chemical
 series, ARE113007, selectively decreased food intake and body weight gain
 after oral administration in food-deprived, free-fed, and diet-induced
 obese rats. ARE113007 also increased lipid utilization and reduced fat
 mass. Together, these data suggest that GPCR ARE113 may be a potential
 novel **receptor** target for the treatment of obesity. To our
 knowledge, this is the first discovery of a behaviorally active small
 molecule with specific inverse agonist activity at an **orphan**
 GPCR without prior identification of natural ligands at that
receptor.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 TI Informatics integration within the drug discovery pipeline at Arena
 Pharmaceuticals
 PY 2001
 SO Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United
 States, April 1-5, 2001 (2001) BTEC-038
 CODEN: 69FZD4

AB Using Constitutively Activated **Receptor** Technol. (**CART**
) Arena Pharmaceuticals is able to screen small mols. against
orphan GPCRs. The drug discovery pipeline at Arena includes the
 identification of novel **orphan** GPCRs from the human genome;
 target validation; HTS and chemical lead expansion. Each of these areas
 requires considerable informatics support. Properly designed enterprise
 information systems can both meet this need and boost productivity by
 providing tools for decision support and real-time communication and
 feedback between the diverse groups of scientists (e.g. screening,
 mol.-biol., in-vivo pharmacol. and chemical). Arena has designed and
 constructed a database system with these criteria in mind: a web-based
 interface provides non-experts with easy access to all Arena's scientific
 data. Different paths into the data allow users appropriate access:
 chemists have access to screening data for their compds.; mol.-biologists

can view gene data and tissue distributions; the lab-scientist can quickly view the results of their experiment and managers can search for leads, generate reports and analyze data. Achieving this goal requires careful attention to users needs and the seamless integration of cheminformatics and bioinformatics.